REMARKS

This document is filed in response to the final office action dated September 10, 2003 ("Office Action"). Claims 1-14 are pending. Reconsideration of this application is requested in view of the following remarks:

Rejection under 35 U.S.C. § 112, first paragraph

The Examiner rejected claims 1-3, 5-6, and 10-14 under 35 U.S.C. § 112, first paragraph on two grounds. Applicants will address each of the grounds below:

I

The Examiner rejected claims 1-3, 5-6, and 10-14 for lack of written description, contending that the specification did not provide support for the phrase "a protein which is involved in replication of the lactic acid bacterial plasmid" recited in claims 1 and 13. See the Office Action, page 4, lines 11-13.

Independent claims 1 and 13 will be discussed first. These two claims are drawn to (1) a Lac shuttle vector containing, among others, a nucleic acid sequence encoding a protein which is involved in replication of the lactic acid bacterial plasmid, and (2) a DNA vaccine containing the vector, respectively.

The Examiner asserted that "the specification provides no limitation on how the protein might be involved in replication of the lactic acid bacterial plasmid, the protein of the claims encompasses any protein that might be considered to be involved in replication of the plasmid." See the Office Action, page 4, line 20 through page 5, line 2.

Applicants would like to point out that the specification discloses a Lac shuttle vector. This vector has a nucleic acid sequence encoding Rep A protein. See, e.g., Examples 2-6 at pages 12-20. It is well known in the art that Rep A protein binds to DNA and is directly involved in bacterial plasmid replication. With this teaching, one skilled in the art would clearly recognize that the claimed vector has a nucleic acid sequence encoding a DNA-binding protein involved in bacterial plasmid replication. Thus, contrary to the Examiner's assertion, the specification does provide a limitation on how the protein might be involved in the lactic acid bacterial plasmid replication, i.e., through binding to DNA. Note that, to satisfy the written description requirement, the specification should be read in light of the knowledge possessed by

those skilled in the art. See, e.g., *In re Lange*, 209 USPQ 294 (CCPA 1981). As pointed out in Applicants' response to the office action filed on June 10, 2003, it is well known in the art that DNA-binding proteins other than RepA are involved in the replication of a naturally occurring and man-made lactic acid bacterial plasmids. Given the knowledge possessed by those skilled in the art, the specification conveys that Applicants were in possession of use of RepA and its equivalents to practice the claimed invention at the time the application was filed.

To further support the rejection, the Examiner asserted that "the protein involved in replication of the lactic acid bacterial plasmid of the instant claims is in no way limited to occurring naturally on lactic acid bacterial plasmids or being structurally related to the proteins disclosed in the art." See the Office Action, page 5, lines 10-12.

Applicants would like to point out that DNA-binding proteins involved in DNA replication are highly conserved among different species throughout evolution. A replication protein of one species often functions well in another species. Also, a mutant of the protein with a non-conserved mutation often functions well too. In other words, a lactic acid bacterial replication protein can be replaced by its counterpart in a different species or its non-conserved mutants, including man-made variants. See, e.g., Kelly et al., Proc. Natl. Acad. Sci. U S A. 1998 Dec 8; 95(25):14634-9 and Brill et al., Mol Cell Biol. 1998 Dec; 18(12):7225-34, attached hereto as "Exhibit A" and "Exhibit B." Accordingly, there is no need to limit the claims as suggested by the Examiner. [1]

For the amendments and reasons set forth above, Applicants submit that claims 1 and 13 meet the written description requirement. By the same token, claims 2-3, 5-6, 10-12, and 14 (dependent from claim 1 or 13) also meet the written description requirement.

II

Claim 13, drawn to a DNA vaccine containing an antigenic gene, remains rejected by the Examiner for lack of enablement. It is the Examiner position that this claim "encompass[es] a DNA vaccine composition comprising any antigenic genes," the majority of which would be

[1] Note that limiting the term "protein" at issue to that "occurring naturally on lactic acid bacterial plasmids" would lead to an unjust result: Others could get around claims 1 and 13 by making a vector or vaccine using a DNA-binding replication protein other than RepA following Applicants teachings, thereby avoiding infringement.

inoperative, and, therefore, undue experimentation would be required to practice the claimed invention. See the Office Action, page 3, line 4 through page 4, line 10.

Applicants disagree. Although some genes may encode antigens that are inoperative (i.e., unable to induce protective immune responses), presence of these genes does not constitute a sufficient ground for non-enablement rejection. As pointed out by the courts,

> the presence of inoperative embodiments within the scope of a claim does not necessarily render a claim nonenabled. The standard is whether a skilled person could determine which embodiments that were conceived, but not yet made, would be inoperative or operative with expenditure of no more effort than is normally required in the art. See, e.g., *Atlas Powder Co. v. E.I. du Pont de Nemours & Co.*, 750 F.2d 1569, 1577, 224 USPQ 409, 414 (Fed. Cir. 1984).

Here, Applicants would like to point out whether a Lac shuttle vector carrying a gene encoding an antigen would be effective in inducing a protective immune response can be evaluated based on the knowledge and methods well known in the art. Inoperative or operative vaccines can be determined "with expenditure of no more effort than is normally required in the art." Thus, claim 13 is enabled.

It is also the Examiner's position that "the teaching in the specification would not enable the skilled artisan to identify the enabled embodiments of the claimed invention without having to ... make and test each and every construct encompassed by the claims." To support his position, he contended that "there is a high degree of unpredictability in the art." See the Office Action, page 3, lines 20 through page 4, line 4.

Applicants would like to bring to the Examiner's attention that it is not necessary to test each vaccine of claim 13 to show its operativeness. The law does not impose such a formidable burden on inventors seeking patent protection. "Appellants (here, Applicants) are **not** required to disclose every species encompassed by their claims **even in an unpredictable art.**" *In re Angstadt*, 190 USPQ 214, 218 (CCPA 1976). Such a holding is only reasonable, since it is very difficult, if not impossible, to test and disclose all operative species in the chemical and biotechnology fields. Indeed, as pointed out by the *Angstadt* court "[w]ithout undue experimentation or effort or expense the combinations which do not work will readily be discovered and, of course, nobody will use them and the claims do no cover them." *Id*, at 219.

For the reasons set forth above, claim 13 has met the enablement requirement

Objection

The Examiner objected to claims 4 and 7-9 as being dependent from rejected claims 1 and 3. As mentioned above, the grounds for rejections of claims 1 and 3 have been overcome. The objection should be withdrawn.

CONCLUSION

Applicants submit that the grounds for rejection and objection asserted by the Examiner have been overcome, and that claims 1-14, as pending, define subject matter that is fully enabled and sufficiently described. On this basis, it is submitted that allowance of this application is proper, and early favorable action is solicited.

Enclosed is a $210 check for the Petition for Extension of Time fee. Please apply any other charges to Deposit Account No. 06-1050, referencing Attorney Docket No. 12875-002001.

Respectfully submitted,

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